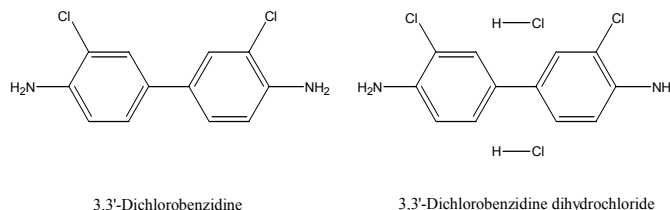


3,3'-DICHLOROBENZIDINE AND 3,3'-DICHLOROBENZIDINE DIHYDROCHLORIDE
CAS Nos. 91-94-1 and 612-83-9

First Listed in the *Second Annual Report on Carcinogens*



CARCINOGENICITY

3,3'-Dichlorobenzidine and 3,3'-dichlorobenzidine dihydrochloride are *reasonably anticipated to be human carcinogens* based on sufficient evidence of carcinogenicity in experimental animals (IARC V.4, 1974; IARC V.29, 1982; IARC S.4, 1982). The generic name 3,3'-dichlorobenzidine is used interchangeably with 3,3'-dichlorobenzidine dihydrochloride. Although only the dihydrochloride salt is believed to be available commercially, it was not always clear whether the salt or the free base was the compound under study. When administered in the diet, 3,3'-dichlorobenzidine induced hepatomas in male mice. When administered in the diet, the compound increased the incidences of granulocytic leukemia and Zymbal gland carcinomas in male rats and mammary adenocarcinomas in rats of both sexes. When administered in the diet, 3,3'-dichlorobenzidine induced transitional cell carcinomas of the urinary bladder in hamsters and female dogs and hepatocellular carcinomas in female dogs. When administered by transplacental exposure, the compound increased the incidences of lymphoid leukemia in mice.

There are no adequate data available to evaluate the carcinogenicity of 3,3'-dichlorobenzidine or 3,3'-dichlorobenzidine dihydrochloride in humans (IARC V.29, 1982; IARC S.4, 1982; IARC S.7, 1987). In three retrospective epidemiological studies, no urinary bladder tumors were reported in men occupationally exposed to 3,3'-dichlorobenzidine, but the studies were inadequate to exclude carcinogenicity.

PROPERTIES

3,3'-Dichlorobenzidine occurs as a gray to purple crystalline solid. It is commercially available in the United States as the dihydrochloride salt with a 60%-67% minimal purity measured as 3,3'-dichlorobenzidine. 3,3'-Dichlorobenzidine dihydrochloride occurs as moist, colorless or white needles or crystals with a mild odor of aromatic amines. 3,3'-Dichlorobenzidine and its dihydrochloride are essentially insoluble in cold water but soluble in ether, benzene, glacial acetic acid, and alcohol. 3,3'-Dichlorobenzidine degrades rapidly in sunlight. When heated to decomposition, these compounds emit toxic fumes of hydrochloric acid and other chlorinated compounds as well as nitrogen oxides (NO_x).

USE

In the United States, 3,3'-dichlorobenzidine is used mainly in the manufacture of pigments for printing ink, textiles, paper, paint, rubber, and plastics and as a curing agent for isocyanate-containing polymers and solid urethane plastics (IARC V.4, 1974; ATSDR, 1997-R041). At least seven synthetic organic pigments, toners, and lakes were produced with 3,3'-dichlorobenzidine dihydrochloride (Kirk-Othmer V.13, 1981). The yellow pigments derived from the chemical and its salts can be used as substitutes for the lead chromate pigments (HSDB, 1998). Use of 3,3'-dichlorobenzidine to synthesize dyes ended in 1986, with the introduction of better dyes from other sources (ATSDR, 1997-R041). Both compounds have also been reported to be used in a color test for the detection of gold (IARC V.29, 1982). 3,3'-Dichlorobenzidine has also found application in the production of tetraminobiphenol, which is used to produce polybenzimidazole. The thermally stable polymer is used in protective clothing, such as a firefighter's apparel and high-temperature gloves (ATSDR, 1997-R041).

PRODUCTION

Current production volumes of 3,3'-dichlorobenzidine are considered confidential by individual companies and therefore are not available (ATSDR, 1997-R041). The 1998 *Chemical Buyers Directory* lists five U.S. suppliers of the dihydrochloride, whereas *Chemyclopedia 98* only lists one supplier (Tilton, 1997; Rodnan, 1997). The 1997 Directory of Chemical Producers identified one producer of 3,3'-dichlorobenzidine hydrochloride (SRIa, 1997). The USITC has identified one U.S. manufacturer of 3,3'-dichlorobenzidine (base and salt) since 1988 producing an undisclosed amount (USITC, 1989-1991, 1993-1995). In 1986 two producers were named (USITC, 1987) and 10 U.S. suppliers of 3,3'-dichlorobenzidine and 3,3'-dichlorobenzidine dihydrochloride were listed (Chem Sources, 1986). The compounds are imported but no current data are available. The latest figures that were found were for 1983, when 1.1 million lb of 3,3'-dichlorobenzidine (base and salt) were imported, and the pigments derived from the chemical totaled approximately 129,000 lb (ATSDR, 1997-R041). In 1980 about 324,000 lb of 3,3'-dichlorobenzidine and its salts were imported. Estimates from the USITC indicate that 208,000 lb of 3,3'-dichlorobenzidine were imported into the United States in 1979. The 1979 TSCA Inventory did not include 3,3'-dichlorobenzidine or its hydrochloride salt. EPA estimated that 1 million to 10 million lb of 3,3'-dichlorobenzidine dihydrochloride were produced in 1977. An estimated 5 million lb of 3,3'-dichlorobenzidine (base and salt) were produced in 1972. The U.S. Tariff Commission reported that combined U.S. production of 3,3'-dichlorobenzidine and its salts in 1971 by three companies amounted to 3.5 million lb. Commercial production of 3,3'-dichlorobenzidine in the United States began in 1938 (IARC V.4, 1974).

EXPOSURE

The primary routes of potential human exposure to 3,3'-dichlorobenzidine and its dihydrochloride are inhalation of airborne dust, ingestion of contaminated well water by those living near hazardous waste sites, and dermal contact, mainly during industrial operations. Occupational exposure to the dihydrochloride has and probably still does occur during its manufacture and conversion to derived pigments (HSDB, 1998). Recent occupational studies, however, have shown that exposure from the use of benzidine-based dyes and pigments may be insignificant. For example, in 1989 no adverse health effects were found among 20 workers in a Japanese facility manufacturing and handling 3,3'-dichlorobenzidine alone (ATSDR, 1997-R041). The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 1,100 workers were possibly exposed to 3,3'-dichlorobenzidine in the workplace (NIOSH,

1976). No data are available on the number of workers potentially exposed to the dihydrochloride.

For the general population the chance of exposure to 3,3'-dichlorobenzidine and its dichloride salt is probably insignificant. Exposure via air, soil, or water is expected to be negligible. Exposure may occur during the use of pressurized spray containers of paints, lacquers, and enamels containing traces of benzidine yellow, an azo dye derived from 3,3'-dichlorobenzidine. However, the greatest chance of exposure is from the improper land disposal of the compounds (ATSDR, 1997-R041).

EPA reported in 1980 that data on the presence of 3,3'-dichlorobenzidine dihydrochloride in the environment are limited; one survey detected 3,3'-dichlorobenzidine dihydrochloride at concentrations of 0.13 to 3.0 mg/L at one 3,3'-dichlorobenzidine production waste disposal site (IARC V.29, 1982). 3,3'-Dichlorobenzidine and its dihydrochloride salt may be released as emissions or in wastewater during their production or use as dye intermediates. Atmospheric emissions of the compound most likely have been reduced as a result of closed-system operations. The Toxic Chemical Release Inventory (EPA) listed 14 industrial facilities that produced, processed or otherwise used 3,3'-dichlorobenzidine in 1988 (TRI, 1990). In compliance with the Community-Right-to-Know Program, the facilities reported releases of 3,3'-dichlorobenzidine to the environment which were estimated to total 1,000 lb. According to the TRI, in 1994 the estimated releases were only 10 lb to air from one large processing facility, which accounted for all of the total reported environmental releases (ATSDR, 1997-R041).

3,3'-Dichlorobenzidine dihydrochloride readily undergoes photolyses in water exposed to sunlight. It has a strong tendency to partition to soils and sediments, reducing the potential for human exposure (ATSDR, 1997-R041). If released into water, the free base will rapidly adsorb to sediment and particulate matter, where it is bound. When released on land, it will bind to soil and possibly react with soil components. If released into the atmosphere, it will probably adsorb to particulate matter and photodegrade. Concentrations of 3,3'-dichlorobenzidine in wastewaters have been estimated to be 10 ppb (maximum) from metal finishing, 2 ppb (maximum, 0.3 ppb average) from nonferrous metals manufacture, 10 ppb (maximum) from paint and ink manufacture, and 3 ppb (maximum) from coal mining (HSDB, 1998). According to CPSC, residual levels or trace impurities of 3,3'-dichlorobenzidine dihydrochloride may be present both in 3,3'-dichlorobenzidine-based dyes and pigments and in the final consumer products; presence of this potential carcinogen, even as a trace contaminant, is cause for concern, although no data are available on the actual levels of impurities in the final products, the potential for consumer exposure, and the potential uptake.

REGULATIONS

There are no regulations that specifically address 3,3'-dichlorobenzidine dihydrochloride. EPA regulates 3,3'-dichlorobenzidine under the Clean Water Act (CWA), Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), Resource Conservation and Recovery Act (RCRA), Superfund Amendments and Reauthorization Act (SARA), and Toxic Substances Control Act (TSCA). Under CWA, EPA published a water quality criteria document for the protection of human health and has proposed a reportable quantity (RQ) of 10 lb for 3,3'-dichlorobenzidine. CERCLA established a final rule RQ of 1 lb. Under RCRA, EPA regulates 3,3'-dichlorobenzidine as a hazardous constituent of waste. It is subject to reporting requirements under SARA. 3,3'-Dichlorobenzidine and its mixtures have been selected for priority consideration for testing under TSCA. FDA classified 3,3'-dichlorobenzidine as a carcinogen but has enacted no regulatory guidelines. OSHA regulates 3,3'-dichlorobenzidine

3,3'-Dichlorobenzidine and 3,3'-Dichlorobenzidine Dihydrochloride (Continued)

requiring personal protective equipment, training, medical surveillance, signs, labeling, and engineering controls. OSHA also regulates 3,3'-dichlorobenzidine, under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-40.